



# Study On The Impact Of Digital Technologies On Tuberculosis

Heba Rummy, Akanksha, Nakul Gupta, Vikas Chauhan\*

IIMT College of Pharmacy, Plot no 19&20, Knowledge Park III, Greater Noida, Uttar Pradesh, India,  
201310

**Abstract:** Background & objectives: In order to meet the ambitious aim set by the Government of India as well as the sustainable development goals (SDG) target for eliminating tuberculosis in 2030, it is important for the healthcare providers to follow and support the patients throughout the treatment for its successful completion. For monitoring the tuberculosis treatment compliance, Digital Adherence Technologies (DATs) play a major role. DATs are digital tools that use mobile phone, computer, or sensor technologies to support the capture of detailed, daily, patient-specific adherence information. DATs provide opportunities for a more patient-centred care model and also help healthcare workers while treating tuberculosis (TB) patients when compared to traditional directly observed therapy. Hence, in this study explored the acceptance and barriers to the use of DATs for monitoring compliance with TB treatment and its possible solutions.

**Methods:** A community-based qualitative study was done in two PHCs in Puducherry, India among TB patients who completed treatment, healthcare providers such as tuberculosis health visitors, staff nurses, and respective medical officers. Thirty participants were interviewed using purposive sampling to explore TB treatment outcomes over two months (Oct-Nov 2023). In-depth interviews were conducted with the help of a separate interview guide consisting of broad, open-ended questions with two primary stimulus questions based on the acceptance and barriers for use of DATs for capturing adherence to TB treatment. The possible solutions for the barriers to the use of DATs were also explored by the healthcare providers. Manual content analysis was done for the qualitative data.

**Interpretation & Conclusions:** Identification of barriers and potential solutions in DATs can help in the successful monitoring and completion of tuberculosis treatment which are crucial towards achieving the tuberculosis elimination goal set by the Government of India as well as the SDG target for elimination by 2030.

**Index Terms** – DOTs, Digital Technologie, VOTs Tb, Tuberculosis.

## I. INTRODUCTION

Tuberculosis (TB) remains one of India's deadliest diseases, significantly contributing to the country's infectious disease burden. According to the World Health Organization (WHO), India accounts for the highest number of TB cases globally, with an estimated annual incidence of 2.8 million cases.

Despite being curable with appropriate treatment, TB management remains challenging due to the prolonged treatment duration, which ranges from six to 24 months. Poor adherence to TB treatment can lead to severe consequences, such as the development of drug resistant TB and an increased risk of relapse, making adherence monitoring crucial for disease control.

In Pondicherry, TB remains a public health concern, with a case notification rate of approximately 150-200 per 100,000 populations. The National TB Elimination Programme (NTEP) in Pondicherry actively monitors TB patients through Directly Observed Therapy (DOT) centres in Primary Health Centres (PHCs), tertiary care hospitals, and private healthcare settings.

However, challenges such as patient migration, stigma, and treatment fatigue impact adherence, increasing the risk of loss to follow up. Reports from the State Tuberculosis Office (STO), Pondicherry, indicate that typically 8-10 patients completed TB treatment monthly in selected PHCs, highlighting the need for improved adherence strategies. To ensure treatment adherence and successful completion, healthcare providers play a vital role in supporting and monitoring patients throughout their treatment journey.

Traditional approaches like DOT have been used for adherence monitoring but often pose logistic challenges for both patients and healthcare workers. To address these barriers, Digital Adherence Technologies (DATs) have emerged as innovative tools for monitoring TB treatment compliance.

DATs utilise mobile phones, computers, and sensor technologies to provide real-time, patient-specific adherence data, enabling a more patient-centred approach. In India, 99DOTS – a low-cost DAT using medication sleeves with hidden phone numbers has been widely deployed to track adherence. Patients confirm their daily medication intake by making a toll-free call, allowing real-time monitoring.

Over 93,000 patients have been enrolled so far in the 99DOTS programme, improving treatment adherence while optimising healthcare resources. However, challenges such as limited mobile access, patient engagement issues, and disruptions caused by the COVID-19 pandemic have affected its scalability.

Other DATs, such as smart pillboxes and Video Observed Treatment (VOT), provide alternative digital solutions to support adherence. Given the importance of adherence in TB control, this study explores the feasibility and acceptability of digital technologies among patients and healthcare providers in supervising TB treatment adherence in Pondicherry.

Additionally, the study examines the role of DATs in India's TB control programme and their potential for integration into routine patient care. Hence, the present study was done to explore the acceptance and barriers of using DATs for TB treatment compliance among patients and healthcare providers in Thirubhuvanai and Thirukanoor PHCs, Puducherry, and identify potential solutions.

### **Epidemiological analysis**

We modelled the SoC compared with the ASCENT interventions between 2023 and 2035, estimating long-term projections of TB incidence and deaths. Outcomes were expressed in the form of cumulative and incremental (intervention vs SoC) incidence and mortality from 2023 to 2035. We compared our results to the End TB Strategy targets.

## HISTORY

TB or illnesses resembling TB have been described from different civilization since ancient times. The earliest such description can be found in Vedas, where TB was referred to as Yakshma meaning wasting disease. Greek, Chinese and Arabic literature also describes TB like disease. Mycobacterium exists on earth since last 150 million years. Typical tubercular vertebral lesions were seen in mummies from the Egyptian pre-dynastic era and Peruvian pre-Colombian era. The first weak evidence of TB.

## TAXONOMY AND DESCRIPTION OF THE GENUS OF TUBERCULOSIS

The **genus responsible for tuberculosis** is **Mycobacterium**, and the specific species that causes tuberculosis in humans is **Mycobacterium tuberculosis**. Below is the **taxonomy** and **description** of the genus and the species related to tuberculosis.

Taxonomic Rank	Name
Domain	Bacteria
Phylum	Actinobacteria
Class	Actinobacteria
Order	Mycobacteriales
Family	Mycobacteriaceae
Genus	<b>Mycobacterium</b>
Species	<b>Mycobacterium tuberculosis</b>

**Table 1: Taxonomy and Description** of the genus and the species related to tuberculosis

### DESCRIPTION OF THE GENUS MYCOBACTERIUM

Mycobacteria are Gram-positive bacteria, though they do not stain well with the traditional Gram stain due to their waxy, lipid-rich cell wall. Instead, they are identified as acid-fast bacilli using Ziehl-Neelsen staining, thanks to the presence of mycolic acids in their cell walls.

These bacteria are non-motile, non-spore-forming, strictly aerobic, and characteristically slow-growing, often taking weeks to form visible colonies. Their unique cell wall makes them hydrophobic and highly resistant to many antibiotics and disinfectants.

While some non-pathogenic species are found in soil and water, pathogenic mycobacteria typically live intracellularly within host macrophages.

Notable species include *Mycobacterium tuberculosis*, the cause of tuberculosis; *M. bovis*, which causes TB in cattle and can infect humans; *M. leprae*, responsible for leprosy; and *Mycobacterium avium* complex (MAC), which causes opportunistic infections, especially in immunocompromised individuals such as AIDS patients.

## DESCRIPTION OF MYCOBACTERIUM TUBERCULOSIS

**Mycobacterium tuberculosis** is an obligate human pathogen that causes tuberculosis (TB), primarily affecting the lungs, though it can also spread to other organs in cases of extrapulmonary TB. The disease is transmitted through airborne droplets released by infected individuals via coughing or sneezing. Its pathogenicity is largely due to several virulence factors, including a complex, lipid-rich cell wall that helps evade immune detection, the ability to survive and replicate within macrophages, and the capacity to remain latent in the host for years before potential reactivation.

Diagnosis of TB involves tests such as the Tuberculin Skin Test (TST) or Interferon-Gamma Release Assays (IGRAs), along with imaging (chest X-ray), sputum smear microscopy, culture, and PCR-based methods like GeneXpert for rapid detection. Treatment requires a long-term antibiotic regimen typically involving isoniazid, rifampin, pyrazinamide, and ethambutol. However, the emergence of multidrug-resistant (MDR-TB) and extensively drug-resistant TB (XDR-TB) presents significant treatment challenges.

### TYPES OF TUBERCULOSIS

There are several **types of tuberculosis (TB)** based on its location in the body, progression of disease, and infection status. Below is a comprehensive breakdown.

**Tuberculosis (TB)** can be classified based on infection status into **Latent TB Infection (LTBI)** and **Active TB Disease**. In LTBI, the bacteria remain in the body in an inactive state, causing no symptoms and not being contagious. However, it can progress to active disease, especially in individuals with weakened immune systems. Diagnosis typically shows a positive TB skin test or IGRA, with a normal chest X-ray and no clinical symptoms. In contrast, active TB involves actively multiplying bacteria, resulting in symptoms such as a persistent cough lasting more than three weeks, chest pain, hemoptysis (coughing up blood), weight loss, fever, night sweats, and fatigue. Active TB, especially when affecting the lungs, is contagious and requires immediate treatment.

Based on the site of infection, TB can be classified as **Pulmonary TB** or **Extrapulmonary TB**. Pulmonary TB is the most common form and affects the lungs, making it highly infectious due to its airborne transmission. Symptoms include chronic cough, chest pain, and blood in the sputum. **Extrapulmonary TB** occurs outside the lungs and is more common in immunocompromised individuals, such as those with HIV. It typically affects organs like lymph nodes, bones, kidneys, or the brain, and is generally not contagious.

Type	Description
<b>Lymph Node TB (Scrofula)</b>	Most common extrapulmonary TB, usually affects cervical
<b>Pleural TB</b>	Affects the pleura (lining of the lungs) causing pleural effusion
<b>Bone and Joint TB (Pott's disease)</b>	Commonly affects the spine; can cause deformity and paralysis
<b>Genitourinary TB</b>	Affects kidneys, bladder, reproductive organs
<b>Meningeal TB (TB Meningitis)</b>	Infection of the meninges (brain covering); can be fatal
<b>Abdominal TB</b>	Affects intestines, liver, peritoneum

Table 2: Common Types of Extrapulmonary TB

**Drug-sensitive TB** responds to standard first-line drugs like isoniazid and rifampin, while **drug-resistant TB** does not and requires more complex treatment.

Type	Description
<b>MDR-TB (Multidrug-Resistant TB)</b>	Resistant to at least isoniazid and rifampin
<b>XDR-TB (Extensively Drug-Resistant TB)</b>	Resistant to isoniazid, rifampin, fluoroquinolones, and at least one second-line injectable drug
<b>RR-TB (Rifampin-Resistant TB)</b>	Resistant to rifampin, with or without resistance to other drugs
<b>TDR-TB (Totally Drug-Resistant TB) (rare)</b>	Resistant to all known TB drugs (not officially recognized by WHO)

Table 3 Description of Drug Resistance

**Miliary TB** is a rare and severe form of tuberculosis where the bacteria spread through the bloodstream to multiple organs, resembling “millet seeds” on a chest X-ray. It can affect the lungs, liver, spleen, brain, and other organs, and is more common in immunocompromised individuals.

Type	Description
<b>Latent TB</b>	No symptoms, not infectious
<b>Active TB</b>	Symptomatic, may be contagious
<b>Pulmonary TB</b>	In the lungs, contagious
<b>Extrapulmonary TB</b>	Outside the lungs, not usually contagious
<b>Miliary TB</b>	Disseminated TB throughout the body
<b>Drug-Resistant TB</b>	Resistant to one or more first/second-line TB drugs

*Table 4: Types of TB with Description*

### Cost-effectiveness analysis

We estimated incremental costs and DALYs averted for the two DAT interventions against the SoC between 2023 and 2035, and compared against an estimated CET range for Ethiopia.

### Patient and public involvement

Patients were involved in the trial component of ASCENT, they were not involved in the development of this model ling analysis. Results have been disseminated to the community advisory board.

### Materials & Methods

This community-based study was conducted in two PHC service areas, Thirubhuvanai and Thirukanoor, under the department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India a tertiary care teaching hospital.

These PHCs were chosen due to their significant burden of TB cases, active participation in India's NTEP, and accessibility for TB treatment adherence interventions. Data collection was conducted over two months, from October 2023 to November 2023. The protocol of the study was submitted to the Institutional Ethics Committee and approval was obtained.

Written informed consent was obtained. All the information collected from the study participants was kept confidential and their privacy was maintained. Administrative approval from State Task Force OR Committee, Puducherry and STO, Puducherry was also obtained before starting data collection. Study design: This was a community-based qualitative study employing in-depth interviews to explore acceptance, barriers, and solutions for DATs in monitoring TB treatment compliance.

This qualitative approach was chosen to provide detailed insights into patient perspectives, healthcare provider challenges, and the feasibility of integrating digital adherence monitoring within the existing TB control framework. Study participants: The study included two key groups such as patients who completed TB treatment in the Thirubhuvanai and Thirukanoor PHC service areas during the study period and healthcare



providers involved in TB management, including tuberculosis health visitors (TBHVs), staff nurses, auxiliary nurse midwives (ANMs)/accredited social health activists (ASHAs), and in-charge medical officers.

This diverse participant selection ensured that varied perspectives on DATs' usability, effectiveness, and challenges were captured. Sample size and sampling strategy: A non-probability purposive sampling technique with maximum variation and key informant sampling was used. Sampling continued until data saturation was achieved, ensuring no new information emerged from additional interviews.

In-depth interviews were conducted with 30 participants, including patients (completed treatment and lost to follow up) and healthcare providers (TBHV, nurses, medical officers). The interviews were conducted by a qualitative researcher with seven years of experience in TB research. Data collection procedure: Patient details were obtained from the STO, Puducherry, including those who completed treatment and those lost to follow-up within the study PHCs. Informed consent was obtained before interviews.

Interviews were conducted in Tamil (patients and health workers) and English (medical officers) at PHCs, patient residences, or convenient locations ensuring privacy. A structured interview guide with open-ended questions focused on acceptance and barriers of DATs, ease of use for both patients and healthcare providers and potential solutions to improve DATs adoption. The PI acted as a note-taker. Interviews were audio-recorded, transcribed verbatim in English, and anonymised.

Thematic analysis was conducted, codes were generated from transcripts, categories were formed by merging similar codes and themes were developed by grouping related categories. To ensure patient confidentiality, no identifiable information was collected during interviews. Data analysis: Manual content analysis was done for the data from the in-depth interview (IDI) technique. The audio recordings of the interviews conducted in 'Tamil' was translated into English and the transcripts were prepared in verbatim. After comparing with the field notes the final transcripts was prepared.

Transcripts were carefully read, revised and proofread in advance. Transcripts were manually coded using inductive/ deductive reasoning to improve interpretation and codes were merged to form categories and categories were further merged to form themes. The results were reported according to the consolidation criteria for reporting qualitative research guidelines.

## **RESULTS**

The study identified four key categories of benefits associated with the use of Digital Adherence Technologies (DATs) in TB treatment monitoring: time efficiency, improved tracking of loss to follow-up, support for NIKSHAY and Direct Benefit Transfer (DBT), and enhanced patient engagement. Healthcare workers reported that SMS reminders from NTEP were particularly helpful in prompting timely treatment initiation and updating bank details. Barriers to DAT use were categorized into patient-related (e.g., illiteracy, lack of phone access, frequent phone changes), health worker-related (e.g., difficulty using the NIKSHAY portal in field conditions), and program-related factors (e.g., poor network, inability to register multiple phone numbers, and technical limitations). Suggested solutions included linking NIKSHAY IDs with Aadhaar to reduce duplication, distributing mobile phones to those in need, appointing ASHA workers for regular home visits, and making the portal more user-friendly. The involvement of family members and policymakers was also identified as crucial for improving adherence and supporting the scale-up of DATs.

**TABLE OF ABBREVIATION**

SDG	SUSTAINABLE DEVELOPMENT GOALS
DATs	DIGITAL ADHERENCE TECHNOLOGIES
TB	TUBERCULOSIS
PHCs	PRIMATY HEALTH CENTRES
VOT	VIDEO OBSERVEDTREATMENT
NTEP	NATIONAL TB ELIMINATION PROGRAMME

**REFERENCES**

- [1] 1 World Health Organisation. Tuberculosis: key facts. 2023. Available: <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>.
- 2 Iseman MD. Tuberculosis therapy: past, present and future. *Eur Respir J* 2002;20:87S–94s.
- 3 Barter DM, Agboola SO, Murray MB, et al. Tuberculosis and poverty: the contribution of patient costs in sub- Saharan Africa--a systematic review. *BMC Public Health* 2012;12:980:1–21.
- 4 Laurence YV, Griffiths UK, Vassall A. Costs to Health Services and the Patient of Treating Tuberculosis: A Systematic Literature Review. *Pharmacoeconomics* 2015;33:939–55.
- 5 Nezenega ZS, Perimal- Lewis L, Maeder AJ. Factors Influencing Patient Adherence to Tuberculosis Treatment in Ethiopia: A Literature Review. *Int J Environ Res Public Health* 2020;17:5626.
- 6 Long Q, Smith H, Zhang T, et al. Patient medical costs for tuberculosis treatment and impact on adherence in China: a systematic review. *BMC Public Health* 2011;11:393:1–9.
- 7 World Health Organisation. Global tuberculosis report 2022. World Health Organisation; 2022. Available: <https://apps.who.int/iris/handle/10665/363752>.
- 8 World Health Organisation. Global tuberculosis report 2021. World Health Organization; 2021. Available: <https://apps.who.int/iris/handle/10665/346387>.
- 9 Ethiopia Ministry of Health. Ethiopia national health accounts report 2019- 20. 2022.
- 10 Deribew AA, Dememew ZG, Alemu KM, et al. TB- related catastrophic costs in Ethiopia. *Public Health Action* 2024;14:71–5.
- 11 Ministry of Health Ethiopia. Tuberculosis and leprosy national strategic plan (tbl- nsp) July 2021 – June 2026. 2020.
- 12 Subbaraman R, de Mondesert L, Musiimenta A, et al. Digital adherence technologies for the management of tuberculosis. *BMJ Glob Health* 2018;3:e001018.
- 13 Velen K, Nguyen T- A, Pham CD, et al. The effect of medication event reminder monitoring on treatment adherence of TB patients. *Int J Tuberc Lung Dis* 2023;27:322–8.
- 14 Burzynski J, Mangan JM, Lam CK, et al. In- Person vs Electronic Directly Observed Therapy for Tuberculosis Treatment Adherence: A Randomized Noninferiority Trial. *JAMA Netw Open* 2022;5:e2144210.
- 15 Liu X, Thompson J, Dong H, et al. Digital adherence technologies to improve tuberculosis treatment outcomes in China: a cluster- randomised superiority trial. *Lancet Glob Health* 2023;11:e693–703.
- 16 Imperial MZ, Nahid P, Phillips PPJ, et al. A patient- level pooled analysis of treatment- shortening regimens for drug- susceptible pulmonary tuberculosis. *Nat Med* 2018;24:1708–15.
- 17 Arinaminpathy N, Chin DP, Sachdeva KS, et al. Modelling the potential impact of adherence technologies on tuberculosis in India. *Int J Tuberc Lung Dis* 2020;24:526–33.
- 18 Ngwatu BK, Nsengiyumva NP, Oxlade O, et al. The impact of digital health technologies on tuberculosis treatment: a systematic review. *Eur Respir J* 2018;51:1701596.
- 19 McQuaid CF, Foster N, Quaife M, et al. Digital adherence technology for TB: focus on livelihoods as well as lives. *Int J Tuberc Lung Dis* 2021;25:416–7.



- 20 Ridho A, Alfian SD, van Boven JFM, et al. Digital Health Technologies to Improve Medication Adherence and Treatment Outcomes in Patients With Tuberculosis: Systematic Review of Randomized Controlled Trials. *J Med Internet Res* 2022;24:e33062.
- 21 Mohamed MS, Zary M, Kafie C, et al. The impact of digital adherence technologies on health outcomes in tuberculosis: a systematic review and meta- analysis. *Infectious Diseases (except HIV/AIDS)* [Preprint].
- 22 Yoeli E, Rathausser J, Bhanot SP, et al. Digital Health Support in Treatment for Tuberculosis. *N Engl J Med* 2019;381:986–7.
- 23 Wei X, Hicks JP, Zhang Z, et al. Effectiveness of a comprehensive package based on electronic medication monitors at improving treatment outcomes among tuberculosis patients in tibet: a multi- centre randomised controlled trial. *ERS Congress 2024 abstracts*; 2024.
- 24 Iribarren S, Beck S, Pearce PF, et al. TextTB: A Mixed Method Pilot Study Evaluating Acceptance, Feasibility, and Exploring Initial Efficacy of a Text Messaging Intervention to Support TB Treatment Adherence. *Tuberc Res Treat* 2013;2013:349394.
- 25 Cattamanchi A, Crowder R, Kityamuwesi A, et al. Digital adherence technology for tuberculosis treatment supervision: A stepped- wedge cluster- randomized trial in Uganda. *PLoS Med* 2021;18:e1003628.
- 26 Bediang G, Stoll B, Elia N, et al. SMS reminders to improve adherence and cure of tuberculosis patients in Cameroon (TB- SMS Cameroon): a randomised controlled trial. *BMC Public Health* 2018;18:583.
- 27 Belknap R, Holland D, Feng P- J, et al. Self- administered Versus Directly Observed Once- Weekly Isoniazid and Rifapentine Treatment of Latent Tuberculosis Infection: A Randomized Trial. *Ann Intern Med* 2017;167:689–97.
- 28 Johnston JC, van der Kop ML, Smillie K, et al. The effect of text messaging on latent tuberculosis treatment adherence: a randomised controlled trial. *Eur Respir J* 2018;51:1701488.
- 29 Ali AOA, Prins MH. Mobile health to improve adherence to tuberculosis treatment in Khartoum state, Sudan. *J Public Health Afr* 2019;10:1101.
- 30 Manyazewal T, Woldeamanuel Y, Fekadu A, et al. Effect of Digital Medication Event Reminder and Monitor- Observed Therapy vs Standard Directly Observed Therapy on Health- Related Quality of Life and Catastrophic Costs in Patients With Tuberculosis: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Netw Open* 2022;5:e2230509.
- 31 Thompson RR, Kityamuwesi A, Kuan A, et al. Cost and Cost- Effectiveness of a Digital Adherence Technology for Tuberculosis Treatment Support in Uganda. *V Health* 2022;25:924–30.
- 32 Yang J, Kim H- Y, Park S, et al. Cost- effectiveness of a medication event monitoring system for tuberculosis management in Morocco. *PLoS ONE* 2022;17:e0267292.
- 33 Bahrainwala L, Knoblauch AM, Andriamiadanarivo A, et al. Drones and digital adherence monitoring for community- based tuberculosis control in remote Madagascar: A cost- effectiveness analysis. *PLoS One* 2020;15:e0235572.
- 34 Nsengiyumva NP, Khan A, Gler MMaTS, et al. Costs of digital adherence technologies for tuberculosis treatment support. *Infectious Diseases (except HIV/AIDS)* [Preprint].
- 35 Tadesse AW, Mohammed Z, Foster N, et al. Evaluation of implementation and effectiveness of digital adherence technology with differentiated care to support tuberculosis treatment adherence and improve treatment outcomes in Ethiopia: a study protocol for a cluster randomised trial. *BMC Infect Dis* 2021;21:1149.
- 36 Foster N, Tadesse AW, McQuaid CF, et al. Evaluating the equity impact and cost- effectiveness of digital adherence technologies with differentiated care to support tuberculosis treatment adherence in Ethiopia: protocol and analysis plan for the health economics component of a cluster randomised trial. *Trials* 2023;24:292.
- 37 Tadesse AW, Sahile M, Foster N, et al. Cluster- randomized trial of digital adherence technologies and differentiated care to reduce poor end- of- treatment outcomes and recurrence among adults with drug- sensitive pulmonary tb in Ethiopia. *Public and Global Health* [Preprint].
- 38 Foster N, Tadesse AW, Belachew M, et al. Equity, cost and disability adjusted life years of tuberculosis treatment supported by digital adherence technologies and differentiated care in ethiopia: a trial- based distributional cost- effectiveness analysis. *Public and Global Health* [Preprint].
- 39 Kebede AH, Alebachew Z, Tsegaye F, et al. The first population- based national tuberculosis prevalence survey in Ethiopia, 2010- 2011. *Int J Tuberc Lung Dis* 2014;18:635–9.
- 40 World Health Organisation. Global tuberculosis programme. 2022. Available: <https://www.who.int/teams/global-tuberculosis-programme/data>.
- 41 Iskauskas A, Vernon I, Goldstein M, et al. Emulation and History Matching using the hmer Package. 2022;220905265.

- 42 Scarponi D, Iskauskas A, Clark RA, et al. Demonstrating multi- country calibration of a tuberculosis model using new history matching and emulation package - hmer. *Epidemics* 2023;43.
- 43 Jerene D, Levy J, van Kalmthout K, et al. Effectiveness of digital adherence technologies in improving tuberculosis treatment outcomes in four countries: a pragmatic cluster randomised trial protocol. *BMJ Open* 2023;13:e068685.
- 44 Ochalek J, Lomas J, Claxton K. Estimating health opportunity costs in low- income and middle- income countries: a novel approach and evidence from cross- country data. *BMJ Glob Health* 2018;3:e000964.
- 45 Menzies NA, Gomez GB, Bozzani F, et al. Cost- effectiveness and resource implications of aggressive action on tuberculosis in China, India, and South Africa: a combined analysis of nine models.

